REMARKS

Claims 1-9, 11, and 23-41 are pending in the application. Claims 10 and 12-22 have been cancelled without prejudice as directed to non-elected inventions. Claims 1-7 and 11 have been amended. New claims 23-41 have been added. Support for the amendments and new claims can be found in the specification at, e.g., page 3, paragraph 0018; page 4, paragraph 0020; page 7, paragraph 0041; page 7, paragraph 0042; page 11, paragraph 0057; page 14, paragraph 0063; and page 21, paragraph 0084. These amendments add no new matter.

The specification has been amended at page 18, paragraph 0075 to correct an obvious error regarding the accession number of deposited ABE3.16 hybridoma. This paragraph has been amended to recite the ATCC accession number "PTA-3350" instead of "PTA-3550." Support for this amendment can be found, e.g., in original claims 2, 3, 8, and 9, and in the specification at page 2, paragraphs 0011 and 0012, and page 10, paragraph 0053, all of which refer to the deposited ABE3.16 hybridoma as having accession number ATCC "PTA-3350." Accordingly, one skilled in the art would recognize the error in the specification as well as the correction made by the present amendment. This amendment adds no new matter.

Specification/Informalities

At page 2 of the Office Action, the Examiner noted several spelling errors in the specification. In response to the Examiner's request, applicants have corrected these errors throughout the specification.

35 U.S.C. §101 (Non-Statutory Subject Matter)

At pages 2-3 of the Office Action, the Examiner rejected claims 1-5 as allegedly being directed to non-statutory subject matter. As amended, claims 1-5 are directed to an "isolated" antibody or antigen-binding fragment thereof. In view of this amendment, applicants request that the Examiner withdraw the rejection.

35 U.S.C. §112, First Paragraph (Enablement)

At page 3-4 of the Office Action, the Examiner rejected claims 1-7 and 11 as allegedly not enabled. According to the Examiner,

> [t]he specification, while being enabling for antibody that binds to an epitope within SEQ ID NO:1,, does not reasonably provide enablement for antibody derivative or antigen binding polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants respectfully traverse the rejection in light of the claim amendments and the following comments.

As amended, the claims are directed to an isolated antibody or an antigen-binding fragment thereof that (i) binds to an epitope within or overlapping the amino acid sequence of SEQ ID NO:1, (ii) has the same epitope specificity as the antibody produced by the hybridoma deposited in the ATCC under Accession No. PTA-3350, or (ii) crossblocks the binding of the antibody produced by the hybridoma deposited in the ATCC under Accession No. PTA-3350.

The claims have been amended to remove the phrases "antibody derivative" and "antigen-binding polypeptide," thereby obviating the Examiner's rejections as directed to these phrases.

As detailed in the passage from the Office Action reproduced above, the Examiner has acknowledged the enablement of an antibody that binds to an epitope within SEQ ID NO:1. In addition, applicants respectfully submit that the skilled artisan would have been able, without undue experimentation, to make and use the full scope of the antibodies and antigen-binding antibody fragments encompassed by the amended claims. At the outset, Applicants note that the Rudikoff paper cited by the Examiner regarding enablement was published in 1982, almost 20 years before the priority date of the present application. Thus, the Rudikoff paper is not at all representative of the state of the art at the time of priority. At the time of the priority date, working knowledge of antibody structure and function was quite well developed. For example, the specification describes (at page 14, paragraph 0063) methods for preparing antigen-binding fragments of antibodies. Such methods include disulfide cross-linking and enzymatic cleavage

(e.g., papain or pepsin digestion) to generate $F_{(ab')2}$, $F_{ab'}$, or F_v fragments. Other methods of preparing antibody fragments include the use of an Fab combinatorial library or a bacteriophage-based expression system to identify a large number of F_{ab} fragments having specificity for a particular antigen (see Huse *et al.* (1989) *Science*, 246:1275-1281, cited in the specification at page 14, paragraph 0063).

In addition to having been able to readily produce antibody fragments, a skilled person would have required no undue experimentation to identify those fragments that retain antigen-binding ability. For example, the skilled artisan would have recognized that enzymatic cleavage of a whole antibody molecule can generate a pool of antibody fragments that retain antigen-binding ability. In those cases where evaluating or confirming the ability of an antibody fragment to bind to an antigen is desirable, it would have been well within the grasp of the skilled artisan to use methods such as an enzyme-linked immunoabsorbance assay (ELISA) to detect binding activity (see, e.g., specification at page 19, paragraph 0079). Using such methods and applying the teachings of the specification, the skilled artisan would have been able to readily prepare and identify antibody fragments that (i) bind to an epitope within or overlapping the amino acid sequence SSDGLWNNNQTQLFLEHS (SEQ ID NO:1), (ii) have the same epitope specificity as the antibody produced by the hybridoma deposited in the ATCC under Accession No. PTA-3350, or (iii) crossblock the binding of the antibody produced by the hybridoma deposited in the ATCC under Accession No. PTA-3350.

In light of the claim amendments and the preceding comments, applicants submit that one of ordinary skill in the art would have been able, at the time of filing of the present application, to make and use the claimed antibodies and antigen-binding fragments without undue experimentation and with a reasonable expectation of success. Accordingly, applicants request that the Examiner withdraw the rejection of independent claims 1-3 and the claims that depend therefrom.

At pages 4-5 of the Office Action, the Examiner rejected claims 3, 8, and 9 as allegedly not enabled. According to the Examiner, it is not apparent whether the ABE3.16 hybridoma is

available to the public and/or whether the hybridoma has been deposited under the terms of the Budapest Treaty.

Applicants note that the specification discloses that the ABE3.16 hybridoma was deposited with the American Type Culture Collection (ATCC) on May 2, 2001 under the terms of the Budapest Treaty (see, e.g., page 10, paragraph 0053 and page 18, paragraph 0075). The deposited hybridoma was assigned the accession number ATCC PTA-3350. A copy of the ATCC deposit receipt is enclosed with this response.

The ATCC has accepted the deposits under the provisions of the Budapest Treaty for the Deposit of Microorganisms, i.e., they will be stored with all the care necessary to keep them viable and uncontaminated for a period of at least thirty (30) years from the date of deposit, five years after the most recent request for a sample of the deposits, or for the enforceable life of the patent, whichever is longer.

Applicants acknowledge the duty to replace the deposits should the depository be unable to furnish a viable sample when requested.

All restrictions on the availability to the public of the subject hybridoma deposits will be irrevocably removed upon the granting of a patent on the present application. The material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 CFR § 1.14 and 35 U.S.C. § 1.22.

In light of these comments and the enclosed receipt of deposit, applicants respectfully request that the Examiner withdraw the rejection of claims 3, 8, and 9.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are now in condition for allowance.

Enclosed is a check for excess claim fees. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 13751-032001.

Respectfully submitted,

Date: April 13, 2005

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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Biogen, Inc.
Attn: Christopher D. Benjamin
14 Cambridge Center
Cambridge, MA 02142

Deposited on Behalf of: Biogen, Inc.

Identification Reference by Depositor:	**Patent Deposit Designation**
Hybridoma: ABE3.16	PTA-3350

The deposit was accompanied by: __ a scientific description __ a proposed taxonomic description indicated above.

The deposit was received May 2, 2001 by this International Depository Authority and has been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested May 8, 2001. On that date, the culture was viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Tanya Nunnally, Patent Specialist, Patent Depository **Date:** May 24, 2001

cc: Gary Creason
(Ref: Biogen document A124P)